CASE REPORTS

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Rapid Resolution of a Pulmonary Embolus in Man

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BASIC TO diagnosis and management in cases of suspected or documented pulmonary emboli is an understanding of the natural history of this disease and its response to treatment. One critical aspect of natural history is definition of the speed with which emboli can resolve. A number of reports have appeared quantitating the rate of resolution of pulmonary emboli during anticoagulant therapy in dogs[1-4] and in man.[5-13] In dogs emboli appear to resolve faster than in humans; the most rapid resolution of a documented embolus reported in man is seven days.[6] We wish to report the case of a patient with massive pulmonary emboli in which one large embolus resolved within 51 hours of the start of heparin therapy.

Report of a Case

A 59-year-old man was admitted to the Veterans Administration Hospital in San Diego on August 19, 1975, because of left-sided weakness for three hours.

He had been in good health until 1971 when he noted the acute onset of left-sided weakness, which resolved partially over the following year. Two weeks before the present admission there was sudden onset of weakness in his left hand and foot, which resolved completely in 30 minutes. On the evening of admission there occurred acute onset of weakness in his left foot and numbness of his left hand, without other symptoms.

He had smoked one pack of cigarettes a day for 20 years but had stopped in 1945. He said that there had been no respiratory symptoms.

On admission he appeared in no distress; temperature taken orally was 36.9°C (98.5°F); heart rate, 100 beats per minute; blood pressure 160/80 mm of mercury, and respirations, 20 per minute. There were no carotid bruits. The chest, heart and abdomen appeared normal. There was no evidence of venous disease in the legs. The left hand and ankle were weak; the remainder of the neurologic examination gave findings within normal limits.

Pertinent negative laboratory data included complete blood count, liver function tests, blood urea nitrogen, blood glucose, electrolytes, prothrombin and partial thromboplastin times, and roentgenogram of the chest.

A diagnosis of an incomplete right middle cerebral artery occlusion was made, and the patient was admitted to the neurology service, where heparin therapy was begun. Attempts at lumbar puncture were unsuccessful. After two days, heparin therapy was discontinued in anticipation of cerebral angiography; however, the patient then noted the development of headaches followed by left hemiparesis, and cerebral angiography was cancelled.

Over the ensuing 19 days the patient was confined to bed and there was little resolution of neurologic deficits. His course was complicated by intermittent spiking fevers of unknown cause, hyperglycemia and hyperosomolarity. He was treated with steroids, glycerol, penicillin, insulin and bronchodilators by intermittent positive pressure. On September 11 he became hypotensive, and subsequently was moved to the medical intensive care unit. On transfer, his temperature was 39.4°C (103°F); blood pressure, 100/60 mm of mercury; heart rate, 120 beats per minute; respirations, 28 per minute. Tubular breath

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sounds were noted in the right middle and lower lung fields, but no rales. A left hemiparesis persisted. Lumbar puncture disclosed xanthochromic fluid with a normal leukocyte count. Arterial oxygen pressure (Po_2) with the patient breathing 100 percent oxygen was 268 mm of mercury; carbon dioxide pressure (Pco_2) was 34 mm of mercury, and pH 7.36. A roentgenogram of the chest was interpreted as showing "minimal haziness" in the right upper lobe. A Gram stain of a transtracheal aspirate showed many polymorphonuclear leukocytes and Gram-negative bacilli. The patient was thought to have either a Gram-negative pneumonia or thromboembolism.

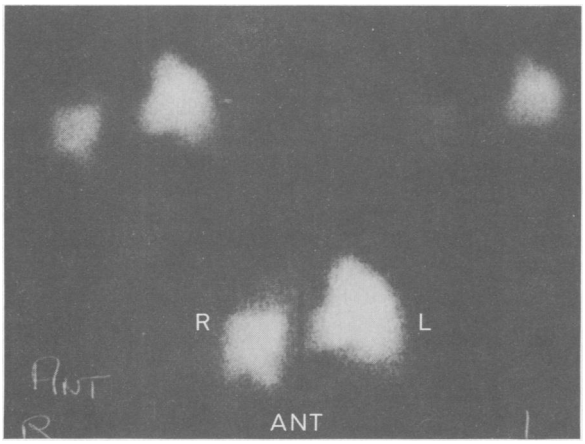

Figure 1.—Technetium 99m perfusion lung scan done September 11, 1975; anterior views. Perfusion defects at the right apex and at the right and left bases are shown.

A technetium 99m perfusion lung scan on September 11, 1975, showed large perfusion defects in both posterior basal regions and in the right upper lung field (Figure 1). Ventilation scanning could not be done because of the patient's critical condition. Because he was considered to be at high risk for resumption of anticoagulant therapy because of probable recent intracerebral bleeding, a pulmonary arteriogram was carried out that evening (ten hours after the onset of hypotension) to clarify the diagnosis (Figure 2). It showed a large embolus in the right pulmonary artery at its bifurcation into upper and lower divisions, with extension into multiple vessels in the right upper lobe; selective injection of the left pulmonary artery showed a large thrombus in the lower divisions with complete cutoff of vessels to the lower lobe. Despite the extensive bilateral emboli, runoff of contrast material from each pulmonary artery was good.

Intravenous administration of heparin was begun (an initial bolus of 10,000 units followed by

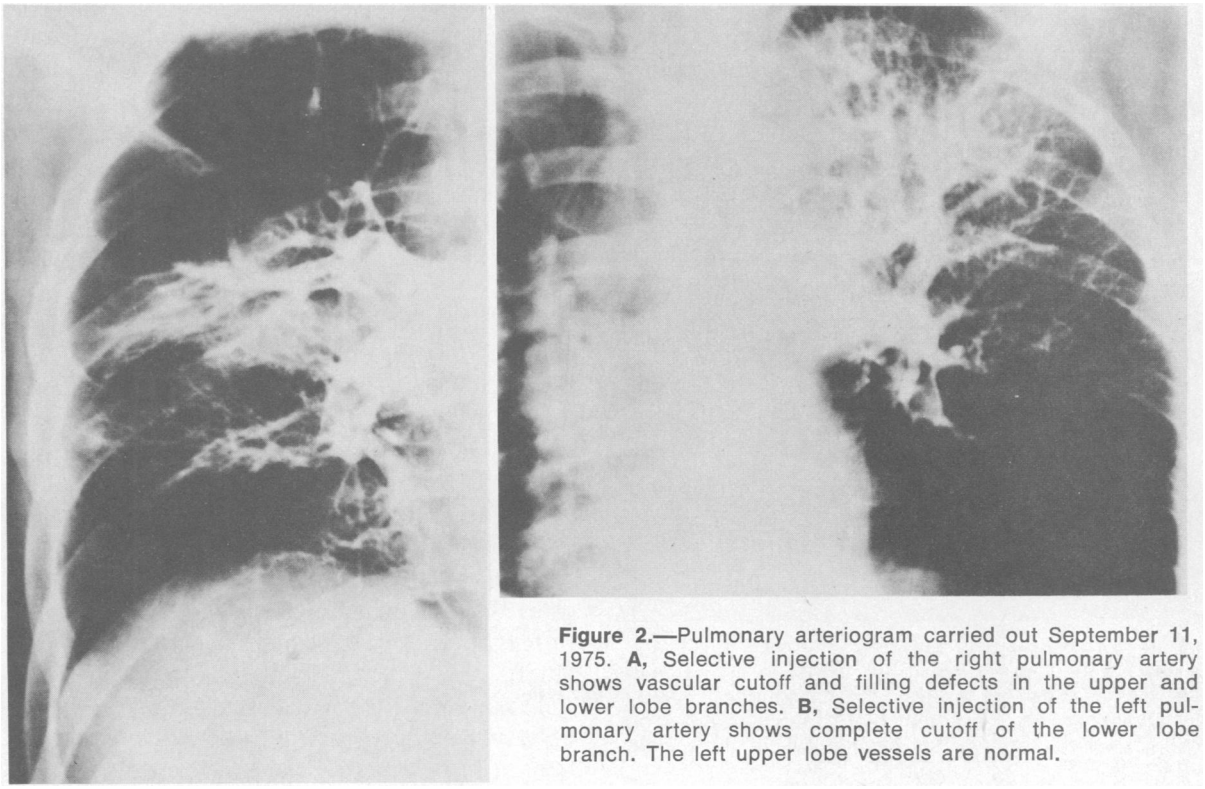

Figure 2.—Pulmonary arteriogram carried out September 11, 1975. **A,** Selective injection of the right pulmonary artery shows vascular cutoff and filling defects in the upper and lower lobe branches. **B,** Selective injection of the left pulmonary artery shows complete cutoff of the lower lobe branch. The left upper lobe vessels are normal.

constant infusion of 1,000 units per hour). A Swan-Ganz catheter with thermodilution sensor was inserted into a right lower lobe arterial branch; the pulmonary artery pressure was 25/7 mm of mercury (mean, 16 mm of mercury). Multiple attempts to measure wedge pressure were unsuccessful. Cardiac output (thermodilution) was 4.1 liters per minute. With 40 percent oxygen given by mask, arterial P_{O_2} was 126 mm of mercury, P_{CO_2} was 35 mm of mercury and pH was 7.36.

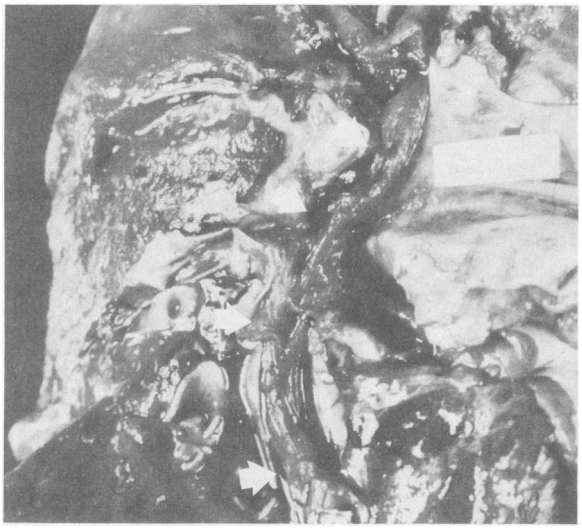

Figure 3.—Appearance at autopsy of the right pulmonary artery thrombus. The pulmonary arterial system has been opened and the right lung and pulmonary artery are viewed from the medial aspect. A large thrombus **(arrows)** is seen filling the right upper and lower lobar branches.

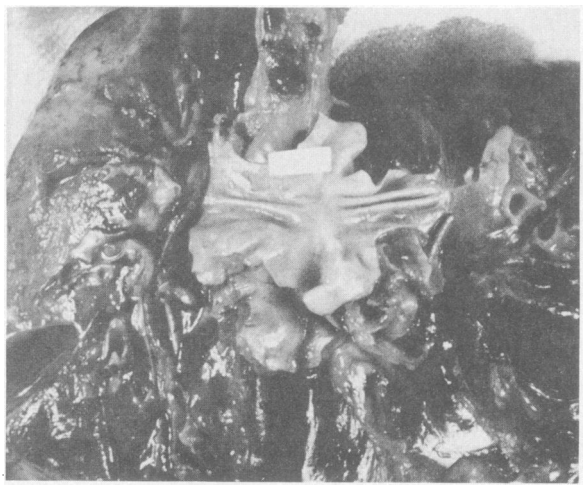

Figure 4.—Appearance at autopsy of the main pulmonary trunk and its branches. The right side is pictured as seen in Figure 3; the left lung and pulmonary artery are viewed from the medial aspect and are seen to be free of thrombi. The trachea lies in the middle of the figure.

Over the next 36 hours, increasingly higher inspired oxygen fractions were required to maintain an adequate arterial P_{O_2}. A roentgenogram of the chest showed persistence of the right upper lobe haziness and a new infiltrate in the right lower lobe. Progressive hypoxia and respiratory acidosis developed, with the arterial P_{CO_2} rising to 55 mm of mercury; elective nasotracheal intubation was carried out, apparently without incident. However, the patient became hypotensive soon after intubation and an idioventricular rhythm developed. Physical findings suggested a left pneumothorax, and a chest tube was inserted.

Attempts to maintain an adequate cardiac output were unsuccessful and the patient died at 5 PM, 51 hours after hypotension was first diagnosed.

At autopsy, attended by the physicians who had managed the patient, the large embolus shown by angiography in the right pulmonary artery was found intact (Figure 3). The macroscopic organization of the clot and its firm adherence to the vascular walls indicated it to be clearly antemortem in origin. The left main pulmonary artery, however, was free of thrombi (Figure 4). Furthermore, extensive dissection of the left pulmonary arterial tree disclosed no macroscopic evidence of antemortem thromboemboli. Hemorrhagic infarctions of both lower lobes, extending to pleural surfaces, were present; a large mural thrombus was found in the right atrium, but no underlying evidence of infarction or injury to the atrial tissue was evident. No breaks in the tracheal, bronchial or pleural surface which might explain the acute left pneumothorax were found.

Discussion

The speed with which pulmonary emboli can resolve has both therapeutic and diagnostic implications. With respect to therapy, speed of resolution is one determinant of the duration of therapy. The twin purposes of anticoagulant therapy in venous thromboembolism are to halt the growth of thromboemboli and reduce the likelihood of recurrence. Resolution of pulmonary emboli indicates that the first objective has been achieved; resolution of venous thrombi helps to achieve the latter.

Diagnostically, embolic resolution rate bears upon two important and frequently-raised questions: (1) how rapidly can an abnormal perfusion

scan secondary to embolism return to normal and (2) how quickly must a pulmonary angiogram be done so that a "false negative" result due to embolic resolution can be avoided?

The case reported here illustrates the fact that resolution, even of major emboli, can occur rather swiftly in man. The documented emboli had resolved completely within 41 hours after the angiogram.

In dogs we have shown that complete resolution of massive fresh emboli can commonly occur within a day, and that the resolution rate is accelerated by administering heparin (presumably because heparin halts thrombus growth and allows the fibrinolytic system to function unopposed).[4]

Data in humans are difficult both to obtain and to quantify precisely. The age of the thrombus before detachment is unknown and aged emboli are known to resolve more slowly than recently-formed emboli.[13,14] Further, the exact time at which the embolus occurred is difficult to pinpoint; therefore, the period between embolism and resolution contains a presumptive element. And, finally, the required sequential observations can be made in man only during rigorously controlled investigational protocols or under unusual clinical circumstances, as in our patient.

The word *resolution* has been used here and in other reports to describe the reduction (or total disappearance) of embolic obstruction, permitting reestablishment of pulmonary blood flow. Resolution does not imply the mechanisms responsible because, in man, it is virtually impossible to distinguish among them if the patient survives. Three mechanisms can lead to resolution: fibrinolysis (dissolution), fragmentation with distal migration of the fragments, and organization. In our patient, autopsy findings documented that resolution of the emboli on the left did not occur by organization; furthermore, no emboli were recovered from the smaller distal vessels by further dissection of the left lower lobe. Consequently, our presumption is that fibrinolysis did occur. But, whatever the mechanism, the central diagnostic fact remains that a large embolus shown to be present by angiogram on one occasion would not have been seen had an angiogram been repeated 41 hours later.

How can it be that one embolus (on the left) resolved while others (on the right) did not? Multiple factors may condition the rate of thrombus resolution, particularly by fibrinolysis.[4] Perhaps the most important factor is the age of the thrombus. It has been shown both experimentally and clinically that older thromboemboli are substantially more resistant to spontaneous or urokinase-induced lysis than are fresh thromboemboli.[13,14] Since the emboli on the right in this patient had undergone some organization, we believe we can construct a rational sequence to explain what occurred in this patient. At some time during the period before the episode of hypotension on September 11, the patient likely had one or more episodes of unrecognized embolization to the right lung which did not resolve. On September 11 an embolic recurrence occurred and the embolus had no alternative but to enter the vessels of the left lung. Our assumption is that this event led to his hypotensive episode. Subsequently, this "fresh" embolus underwent dissolution, perhaps enhanced by institution of heparin therapy.[4] Assumption of such a sequence seems justified in this patient, particularly since we have previously documented that different rates of embolic resolution do occur in man.[16]

Previous reports of resolution of pulmonary emboli in man have used repetitive perfusion lung scanning,[9,10] pulmonary angiography,[5-7] or both,[8,11,13] to document and quantify degrees of resolution. Poe and co-workers reported the earliest resolution of blood flow through an occluded lobar artery in man in four days, based on scan.[9] Almost all of their patients were receiving heparin, and, as was done here and in the Urokinase Pulmonary Embolism study, the recovery of perfusion was timed from the onset of symptoms, presumably coinciding with the occurrence of the embolic event. Complete resolution of angiographic evidence of thromboembolism has occurred after 7 days of heparin therapy in a patient in one report[6] and 14 days in a patient in another.[12]

The perfusion scan and the pulmonary angiogram do not, of course, provide the same data regarding resolution rates. The scan documents return of blood flow, not restoration of total luminal patency. Normal distal blood flow occurs when 20 percent or more of the pulmonary artery lumen has been restored.[15] Therefore, the findings on scan can return to normal when an angiogram still shows a significant luminal filling defect, as we have shown.[16]

The present case, based on angiographic and autopsy observations, does not suffer from such

interpretive limitations. Clearly, emboli can resolve in man within the time period reported here. How often resolution occurs at this rate—or within a shorter span of time—remains to be defined. Each such case will further expand our ability to define the time-based rate of embolic resolution more clearly.

Summary

A 59-year-old man admitted to hospital with intracerebral bleeding was shown to have massive pulmonary thromboemboli in the right upper, right lower and left lower pulmonary arterial lobar branches by perfusion lung scanning and by pulmonary angiography. Anticoagulation with heparin was begun but death occurred two days later. At autopsy, the right-sided emboli were intact but no evidence of emboli in the left pulmonary arterial circulation was present. Since death occurred 51 hours after onset of symptoms suggesting pulmonary thromboembolism, this represents the most rapid resolution of a pulmonary embolus reported in man.

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Anorectal Lesions and Syphilitic Hepatitis

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ABBREVIATIONS USED IN TEXT

CSF = cerebrospinal fluid
FTA-ABS = fluorescent treponemal antibody absorption test
RPR = rapid plasma reagin (test)

CLINICALLY APPARENT HEPATITIS is an uncommon manifestation of secondary syphilis. When hepatic dysfunction is the major feature of syphilis, it may be difficult to recognize the cause, particularly when primary lesions are covert or occur in unfamiliar locations. The following case illustrates such an occurrence.

Report of a Case

A 33-year-old previously healthy man noted the development of painful defecation without change in stool character while he was in Korea in November 1975. Approximately two weeks later he was admitted to an Army hospital in Korea where sigmoidoscopy done under general anaesthesia showed the presence of a "small lesion" at the anal verge, a 1 cm "lesion" in the distal rectum and a 2 cm "mass" at 8 cm. Digital examination disclosed enlarged lymph nodes at the pelvic inlet. A rapid plasma reagin test (RPR) done on December 2 was positive, but a repeat RPR and a fluorescent treponemal antibody absorption test (FTA-ABS) on December 9 were

The opinions or assertions contained herein are the private views of the authors and are not to be construed as reflecting the views of the Department of the Army or the Department of Defense.

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